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GENERAL ARTICLES

RECENT ADVANCES IN REHABILITATING THE TUBERCULOUS*

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From Preston Hall Village Settlement

In these days, when the inclusion of some form of occupational therapy in the treatment of most tuberculous patients is the rule rather than the exception, it is not easy to appreciate the great struggle that pioneers like Marcus Paterson had to make to overcome the prejudice against allowing such patients to do even such minor tasks as putting on footwear without assistance. It was indeed a great triumph to excavate and build the reservoir and the sunk garden at Frimley Sanatorium by patients' labour when it was thought by so many that the slightest exertion entailed a risk of hæmoptysis. Although the theory of treatment by auto-inoculation may have been incorrect, the practice of graduated rest and exercises established the axiom that the tuberculous patient could work and at the same time recover from his disability, provided that the work was suitable and was carried out under medical supervision.

Great as were the advances which Paterson made, they did not provide the solution to the problem of employing the patient. The graduated labour performed at Frimley had little or no productive value and by it the creative instinct of the man could rarely be satisfied. It was therefore left to Sir Robert Philip and Sir Pendrill Varrier Jones to conceive the idea of allowing patients to do useful remunerative productive work.

The Development of the Village Settlement

As long ago as 1910, Philip at the Southfield Colony, near Edinburgh, was the first person to combine treatment with remunerative employment, but these efforts were still chained to the notion that the tuberculous must be given out-door work; the defeat of this cherished idea was due to the foresight and financial genius of Varrier Jones. He realised that treatment was of no avail unless the economic problem was also solved. He, therefore, very boldly, employed the patients in work under industrial conditions whilst they were receiving treatment. With the help of voluntary

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organisations, local authorities, and a team of enthusiastic assistants, both medical and lay, the vision of Varrier Jones materialised into the village settlement.

The formation of a village around the industries was a natural corollary of the principle of providing conditions which would solve the patient's economic, domestic, and social difficulties. It was the fullest possible application of the principle of treating the family as well as the patient, and if we lived in an ideal world where everybody did that which was most beneficial for themselves and others, there is no doubt that the village settlement would be the answer to the tuberculosis problem. But, unfortunately, man is an irrational being, with likes and dislikes, prejudices and weaknesses, so much so that no one scheme can suit the varied demands of a population that has a right to choose its own way of living.

This personal equation mitigates the success of the village settlement programme which can only cater for those who elect to live in rural surroundings and join a population which, although given every opportunity of becoming a normal community, remains a select group, bound together by the ties of a common disability.

Problems of Village Settlements

For years there seemed to be no answer to the problem. Either the man and his family had to accept the conditions of a village settlement with the prospect of a considerable increase in length of life and with good remunerative employment, or he had to fend for himself, taking the risk of relapse and possibly a short life as the price of an environment that gave him the joys of living as he understood them. The majority chose the latter and found employment of doubtful suitability. If by careless habits they spread the tubercle bacillus wherever they resided, they remained a menace to the nation's children and adolescents. Those who accepted the advantages offered by the village settlement were fortunate, for much money had to be spent on them by the local authority to effect their rehabilitation, in fact this expenditure, and the high cost of establishing an industrial colony, were the main reasons why local authorities, with one exception, refrained from embarking on the venture which, although theoretically correct, gave such limited return due to causes impossible of control. On the other hand, during the inter-war years, the financial position of both Papworth and Preston Hall remained precarious. The difficulty of giving the man an adequate wage, when his working capacity was below normal, was one that could not be solved without a heavy subsidy, and this is still and always will be the major problem in employing the individual disabled by respiratory tuberculosis. Great credit must be given to Varrier Jones and to McDougall, who, in spite of serious financial difficulties, fought on and gradually expanded their settlements in the face of much opposition and criticism from both the medical and industrial world. Although both pursued the same aim, these two pioneers worked on different principles. At Papworth, Varrier Jones considered that permanent settlement of the man and his family was necessary for the final rehabilitation of the patient, but at Preston Hall, McDougall did not regard this as the ultimate goal. He did not consider rehabilitation complete until the man

and his family were living again among the normal population, and the patient had been once again absorbed into normal or sheltered industry outside the industrial colony. He did, however, realise that this took time and that it was necessary to provide living accommodation for patients and their families during the period of rehabilitation; but such accommodation was not regarded as permanent, but only for the time required to obtain the maximum degree of working capacity and technical skill to ensure a reasonable chance of employment in the outside industrial world. Such a project is not so fantastic as might at first appear. England[1] has shown that in Oxfordshire 62 per cent. of a series of 288 tuberculous males on the tuberculosis register were working in normal industry. This figure has been confirmed by Hardy,[2] who found 47 per cent. of 388 males in the Hull area working, and 57 per cent. of 1,055 males at Uxbridge.[3] It is reasonable to assume that with a well-regulated rehabilitation course, this figure might be increased.

Unfortunately, there are no adequate statistics to show the true value of our rehabilitation schemes. It would be very helpful to know what proportion of all admissions to village settlements have become temporary or permanent settlers and how the length of life of these compares with a clinically similar group who have returned to domiciliary care on discharge from treatment at a sanatorium and have been employed in similar occupations. The total cost of treatment and rehabilitation of these two groups would also be enlightening. Much of what has been written about rehabilitation, and I plead guilty myself, is based on mere impressions; we have practically no proof up to the present that we have pursued the best and most economical course in our tuberculosis rehabilitation schemes.

You will remind me that there is a large number who will never reach the stage of fitness to be employed in normal or sheltered industry whilst living at home under ordinary conditions, however long they may remain at a rehabilitation centre. To that I fully agree, but I can assure you that such severely disabled persons are as serious a difficulty within the village settlement as outside it. Only rarely do such persons reach the stage of colonisation and become eligible for a cottage in the village, because the absorption of individuals with only a limited expectation of life creates numerous difficulties for the administrators of a settlement. Not only are they a serious financial burden, but if they are married there is the added responsibility, particularly at present, of providing in due course accommodation for the patient's widow as the length of life of this type of colonist is usually shorter than that of his wife.

On the other hand, it is not desirable that the patient who can obtain suitable and safe employment in normal industry, and can live among his fellow workmen without being a menance or danger to the community, should occupy with his family valuable accommodation in an industrial village settlement and thereby prevent the admission of a man who requires sheltered employment with social and domestic assistance for his family. In other words, the arrested case, although valuable to the industrial side of the settlement, is out of place in a residential scheme for the rehabilitation of the disabled. It will, of course, be necessary to retain the services of some arrested cases if they occupy key positions, but the number should not exceed 15 per cent. of the total numbers of settlers. It should therefore be appreciated that only a

certain category of patients can be retained if the settlement is to be used to the best advantage. These are the patients who need permanent sheltered employment and have a reasonable prognosis. When one considers that only a small percentage of this category will accept residence in a village settlement, it is obvious that some other organisation must be established to complete the answer to the tuberculosis rehabilitation problem.

The Influence of the War

These were some of the problems met in the development of industrial village settlements before the war when the struggle for existence was a grim financial battle. Then came the war. Production had to be pressed to a maximum and the demand for labour reached a premium. Orders piled up at all the industrial settlements and to fulfil contracts healthy workers had to be introduced in considerable numbers. Overdrafts were turned into credit balances and the wheels of industry revolved faster and faster as the demand increased. This inclusion of a considerable proportion of healthy labour into the workshops of village settlements has had a marked effect on the policy underlying the function of such establishments. Previously the main idea was to employ the tuberculous to develop industries, but a tendency arose to develop great industries in which the tuberculous might be employed. When proper precautions are taken, one need have little fear from the risk of infection when mixing healthy and tuberculous persons in the same workshop, but there is a danger of the production rate of the healthy worker being too high for the tuberculous person to maintain. If such a course is adopted, the closest medical supervision is therefore necessary to prevent overstraining of the disabled person, who will naturally wish to keep pace with the healthy worker and attempt to earn the same wage. It is necessary to realise the differences between a rehabilitation workshop and a normal factory. These may be summarised in tabular form:

Ordinary Factory.	*Rehabilitation Centre.*
Employees are selected on the grounds of efficiency, good health, and full working capacity.	Rehabilitants are all handicapped by a disability. When the employee is able to do full and normal work, he is encouraged to seek work in the ordinary factory to make place for a disabled person needing help.
Results are measured by the return on the capital invested.	All types have to be engaged, both inefficient and unskilled workers. Results are judged by the number of persons rehabilitated.
Production can be speeded up by faster work and more efficient machinery.	Production cannot be greater than the limited capacity and adaptability of the workers. The machinery has to fit the disability of the operator.
The management desires as few changes as possible in the employees.	The personnel must continually change to benefit the greatest possible number of disabled persons.
The workers are expected to earn their wages.	The rehabilitant has a production capacity much below normal and yet must be paid an adequate wage.

As the war gathered momentum, throughout the country more and more man-power was pressed into service, and the Government realised that there was a reservoir of labour in the disabled. This could be safely tapped if proper

methods were used, not only to the benefit of the nation, but also to the advantage of the disabled person who could be encouraged to work and be suitably remunerated.

Recent Legislation

The first step was the introduction of Memorandum 266T, whereby financial assistance could be given to recoverable cases of respiratory tuberculosis, working part-time on account of their disability, up to eighteen months after discharge from sanatorium treatment. Curiously enough, this measure worked in some instances to the disadvantage of industrial village settlements in that the man who relapsed found that under 266T allowances he was receiving only 10s. less per week than when he was on the maximum hours he was allowed to work in the industries. It became in certain cases a problem to persuade a patient to return to work for the extra 10s. he would receive to the amount granted to him if he remained on allowances. Nevertheless, the granting of financial allowances was a notable advance, and although the memorandum contained many anomalies, it was a valuable piece of legislation which, I hope, will be recognised under the National Insurance Act, and the opportunity taken to improve the condition of all tuberculous persons and not only a selected group.

The second step was taken by the Ministry of Labour and National Service by the introduction of the Disabled Persons Employment Act. This was passed in 1944, and the full benefit of this important Act has not yet been appreciated, in fact, we are only at the beginning of the new era in rehabilitation, one in which, I think, will be developed schemes that will widen the available facilities to include all those unfortunate persons who, either through their temperament or their physical condition, are unable to obtain residence in a village settlement. The patient within the settlement will also be benefited in that it will now be possible to train him with the assistance of the Ministry of Labour and National Service into a skilled workman, able to compete in efficiency and aptitude with his healthy fellows.

Previously, the main object of industrial settlements and sheltered workshops, was to provide the man with suitable employment, an adequate wage and accommodation for him and his family. This was deemed sufficient until the end of the war when large numbers of men came out of the services with tuberculosis but without a trade or vocation. These men not only needed healing, but also training in an occupation by which they would be able to earn a living and look forward to a progressive future as their health became stabilised.

Development of Training Schemes

Many deputations and interviews took place between the various Ministries concerned, the Tuberculosis Rehabilitation Council and the Directors of Village Settlements, in order to establish a residential training scheme for the tuberculous with the same advantages available for the non-tuberculous at the Ministry of Labour and National Service Centre at Egham and the other Government Training Centres. The main difficulty to be overcome was the limited capacity for work and the precarious health standard of the tuberculous compared with other disabled persons, making the problem longer and more

complicated. It was eventually agreed that the length of the training period for the tuberculous should be up to two years, and that during that period the man and his family should be entitled to the Ministry of Labour's training grant. The Training Centre also obtains a Deficiency Allowance on a *per capita* basis.

At Preston Hall a training scheme has been in operation for some months. It has been found necessary to divide it into three phases.

1. *The Stage of Assessment*

This takes place in the wards and begins as soon as the clinical condition allows. It is under the control of the Medical Officer, the Vocational Guidance Officer, and a trained Occupational Therapist. By careful and judicious use of handicrafts and aptitude tests over a period from two to four months, it is possible to assess the suitability of the man for training and also the occupation in which the man is likely to be most successful. When he is up most of the day, the second stage begins.

2. *The Stage of Testing*

During this period the findings and conclusions of the previous team of observers are put to a practical test by introducing the man to the industrial environment of the workshops and at the same time providing him with a course of general education which is essential in the majority of instances if the man is to obtain the full benefit from the third phase.

3. *The Stage of Special Training*

Provided the clinical condition allows, the man now enters on his training course in the specific occupation in which it is hoped he will become proficient and eventually earn his living either in normal industry or a sheltered workshop. This training is undertaken by skilled instructors and takes up to two years during which time the man will be given extended privileges according to his clinical condition. Training is given in carpentry and joinery, building maintenance, printing, clerical work and nursing, and the curriculum of each course has the approval of the Ministry.

It has been necessary to establish a liaison officer between the medical staff, the instructors and the patient. This person, the Training Officer, is in charge of the man's progress and acts very much as a tutor or supervisor of studies does in a collegiate establishment. He has to be selected with care, as it is important that he has the confidence of the staff, and particularly that of the patient, who can confide his difficulties in him.

By this scheme, I hope to be able to overcome that very real criticism of tuberculous industrial settlements—that they provide employment but no future for the disabled in that the work is routine mass production and only can end in a dead-end job. Certain adjustments have still to be made for the previously trained man with intelligence who must find suitable employment when his disease is quiescent; but generally the scheme opens up a new future for the average patient with the hope of rising to a position of responsibility and skilled employment.

There will be many who cannot or do not wish to be trained, and the rise

in incidence of the disease in the older age groups will increase these numbers. For these, there is no alternative at present but to pass them through the workshops giving them graduated employment until the maximum improvement in health has been reached and a state of equilibrium has been obtained between the clinical condition and the productive capacity. It will then be necessary to decide if the man shall be permanently absorbed in the village settlement or return to domiciliary care under the local health authority. Such a return brings us to the care and rehabilitation of the man who resides at home and does not wish to settle in an industrial colony. There are many of these persons and a large number of them have tubercle bacilli in the sputum.

Domiciliary Rehabilitation

Under the 1944 Act, the Minister of Labour and National Service was empowered to assist non-profit-making companies for the employment of the disabled. The Disabled Persons Employment Corporation Ltd. was, therefore, formed, and is taking an active interest in the employment of the tuberculous person living at home.

The positive case should not be employed in normal industry unless special conditions are avilable to meet the criticism and fears of the other workers and to enable the disabled person to work within the limits of his strength. Such conditions can only be provided by large firms, and as the majority of all workers are employed in firms employing less than 200 persons, it is necessary to establish special workshops if the majority of tuberculous persons are to find the necessary conditions to meet their special needs.

In London, such a workshop is already employing over sixty tuberculous persons, the plans for a second at Birmingham are well matured, and two others are contemplated. Good as the scheme is up to the present, there are difficulties which have yet to be overcome. These are mainly financial with respect to meeting the considerable absenteeism which is unavoidable when employing the tuberculous. At the Spero factory in London during the two months ending February 15, 1948, when the maximum possible attendance of all employees at the factory was 2,730 days, absence on account of sickness for which no wages were payable amounted to 596 days. Much of this absence was due to the men having to attend the chest clinic for treatment, at other times it was due to minor ailments of a temporary character. As the Disabled Persons Employment Corporation only pays for the hours worked, financial assistance is needed to meet the hours lost through illness or attendance for treatment. The allowances under memo 266T, sickness benefit if available or social welfare contributions meet the case, but only after the lapse of three or four days. There is, therefore, a period of temporary destitution not covered by any statutory funds when the man undergoes considerable hardship. The solution of this problem has yet to be found.

Although we may provide the most satisfactory form of employment for the tuberculous under ideal industrial conditions, they will be of little avail unless we look to his home environment and ensure that the good work done by providing for his industrial rehabilitation is not undone by poor living conditions.

The village settlement answers this problem completely, but usually the

man wants the old associations of his home and friends; he wants his cinema, his pub without the green fields, the village hall, and the cottage in the country. So long as this desire exists it has to be met, and accommodation must be found near the special workshops that will be acceptable to these people. It is not necessary for me to enlarge upon the difficulties of housing, nevertheless, it is important to have a policy to follow which can be developed as the situation improves.

There are many difficulties attached to the " hostel special factory scheme," the main ones being provision of immediate accommodation for employees who relapse, and finding suitable buildings to be converted into factory-hostels.

But there is little doubt that by careful selection of cases, much of our sanatorium accommodation could be relieved of employable patients by these means without changing their ultimate prognoses. It is a means of attacking the tuberculosis accommodation problem without taxing the already over-strained nursing staff.

Finance

I would not like you to imagine that the rehabilitation schemes that have been described can be carried out without considerable expenditure. Tuberculosis schemes with a good rehabilitation programme are expensive, but they are more expensive without it.

Taking the average case as needing eight months' sanatorium treatment at £5 10s. per week, one and a half years' training at £3 10s. per week—which allows for some productive effort during training—and then a working capacity of 75 per cent. normal for another year before full productive labour can be obtaned, needing a subsidy of about 30s. per week; the treatment and rehabilitation of such a successful case will amount to *at least* £500 at present prices. If there are, as many of us suppose, about 30,000 tuberculous persons needing this service, it is necessary to provide a minimum of £1½ million to carry it through, but even if it costs £2 million, it would be cheap at the price, for the total value of the results cannot be measured in terms of finance. There would be great assets in the form of prevention of spread of infection, homes rescued from breaking up, a higher standard of living for disabled persons and, what is greatest of all, a feeling of confidence, hope and self-respect instilled into tuberculous persons who at present see little else in the future except a life dependent on public charities, frustration of hopes and ambitions, and worst of all, ostracisation by fellow men.

We have now the means to end all this, and by efficient team work we can give the tuberculous hope and confidence to build up homes with the assurance that they shall not be penalised because of their disability. Unfortunately, the schemes laid down by those in charge of tuberculosis rehabilitation centres have been considerably disturbed by the introduction of the National Health Service Act whereby the treatment of a patient is being administratively separated from post-sanatorium rehabilitation. It has always been a principle that rehabilitation is one continuous process that begins as soon as the course of treatment is formulated and develops as the patient recovers from his disability. In practice, this principle must always be followed. Difficulties

will arise if an artificial break in the sequence of events is made by separating hospital from post-hospital rehabilitation.

Those in charge of village settlements will do their best to work under the new conditions imposed by the Act, but they would have preferred to retain and develop their establishments on the lines that past experience has proved to be satisfactory for the tuberculous persons under their care.

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THE CHICK-EMBRYO IN SANATORIUM PRACTICE

BY J. CUTHBERT AND G. G. DAVIDSON

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GUINEA-PIGS and rabbits have hitherto been the animals of choice in laboratory work. They are difficult to obtain at present and, moreover, a licence is necessary for their use. In the cultivation of viruses extensive use is made of the developing chick-embryo as a living culture medium. Beveridge and Burnet (1946) give a bibliography of some 342 works. The subjects covered in this comprehensive list include the technique of inoculation and egg management, the focal lesions on the chorio-allantoic membranes, the cultivation of individual viruses, the cultivation of bacteria, protozoa and foreign tissues in chick-embryos and the cultivation of normal and neoplastic tissues on the chick-embryo. Thus the use of developing chick-embryo is not a novelty but a well-established method in virus work, *e.g.*,

(*a*) in the production of vaccines for prophylactic use (typhus vaccines, yellow fever vaccines, etc.);
(*b*) in producing the reagents for tests like the Frei test, etc.;
(*c*) in diagnosing virus diseases by isolating the virus and noting its cultural characteristics—*e.g.*, comparing chickenpox with smallpox.

Eggs are relatively cheap compared with guinea-pigs and can be easily hatched in any laboratory incubator. Moreover, no licence is necessary to inoculate them before they hatch, provided that none after inoculation are permitted to go to full term. The requirements are a regular supply of fertile hen eggs under 10 days from being laid, preferably not over 3 days old. They should, if possible, be white for ease in candling. An ordinary bacteriological incubator with thermostatic control will hatch out hen eggs at 37·3° C. to 37·8° C. in 21 days. After the first week it is advisable to spray the eggs lightly with a fine mist of warm water from a De Vilbiss spray, each day. The eggs should also be turned daily.

In order to tell whether or not the embryo is alive, trans-illumination or candling is used. A cardboard box containing an electric bulb has an oval

hole, slightly smaller than the perimeter of an egg, cut in its side. The room may be darkened or it will suffice for the operator to sit at the bench and allow a black cloth to enclose his head and shoulders and the box in front of him. By viewing the egg with the oval slit of light behind it, the contents can be made out and the air space, chorio-allantoic blood vessels and presence or absence of embryonic movements easily seen.

A brief description of the development of a chick-embryo will clarify the subsequent remarks. At an early stage three primary layers develop over one pole of the yolk—*i.e.*, ectoderm, mesoderm and entoderm—and the lateral part of the cellular area is differentiated into the dorsal somatopleure and the ventral splanchnopleure. The somatopleure is comprised of ectoderm and mesoderm, while entoderm and mesoderm make the splanchnopleure. The primitive body cavity lies between. The somatopleure folds and overgrows and forms two membranes, the chorion and the amnion. The chorion rapidly lines the egg in close contact with the shell membrane, which it almost completely covers by the tenth day. The amnion completely covers the embryo from the fifth day onwards, except for a small stalk, the yolk stalk. About the third day of incubation the allantois arises from the ventral wall of the primitive hind-gut and grows out into the extra-embryonic body cavity. Lined with entodermal tissue, it has on its outside mesoderm, which latter fuses, as the allantois grows, with the boundaries of the extra-embryonic body cavity. Thus it fuses with the chorion under the shell membrane to form the chorio-allantoic membrane (of which we shall hear more) and internally it fuses with the amnion. Fig. 1 is a dissection of a 10-day embryo fixed in formalin. The air space at the blunt end of the egg is clearly seen. Chorio-allantoic membrane lines the egg and the probe indicates the embryo in the amniotic sac. The store of yolk is plainly visible. The chorio-allantois is the respiratory organ of the embryo and is richly supplied with blood vessels.

Review of Literature

As far as we can ascertain, the chorio-allantois has been used almost exclusively by those studying the growth of acid-fast bacilli in embryos. Levaditi (1906) is credited with being the first to use the chorio-allantoic membrane of chick-embryos as a medium to study bacteria when he worked on the spirillum of fowls. Goodpasture and Anderson (1937) studied the reaction of the chorio-allantoic membrane to various bacteria, *e.g.*, *Staph. aureus*, *Str. Hæmolyticus* and *viridans*, *A. aerogenes*, *E. typhi*, *Br. abortus*, *C. diphtheria* and *M. tub.* (Avian). *M. tuberculosis avium* was shown to be one of the organisms able to utilise a living, intracellular environment for growth. The method of inoculating chorio-allantoic membranes with bacteria was shown to be a practical one for studying phagocytosis and many other problems of infection, especially in the early stages. Costil and Bloch in two classical papers in 1938 described the events on inoculating 10-day chorio-allantoic membranes with human, avian and bovine tubercle bacilli. They describe clearly the naked-eye and microscopic appearances of the nodules which appear after human and bovine tubercle bacilli inoculation. A " reticulo-leucocytic " reaction was evident on the third day and the microscopic lesions clearly visible by the seventh day. There was no essential difference between the membrane's response

to human or bovine strains of *Myco. tub.* Moore had with others made a study of pathogenic fungi and had used the developing chick as a medium for their cultivation. In 1940 he described studies made with *Myco. tub. hominis*, *Myco. tub. bovis*, *Myco. tub. avium*, *Mycobact. marinum* (fish), *Mycobact. thamnopheos* (snake) and *Myco. lepræ muris* (rat). His best results were with 12-day embryos and massive implantations with high concentrations of the bacilli. He concluded that with human type tubercle bacilli the degree of tubercle formation depended on the virulence of the organisms. All the organisms studied were capable of producing lesions and Moore differentiated the chorio-allantoic membrane's reactions to each type of organism. Moore believed that the type of reaction and the degree of response of the membrane to the inoculum served to determine virulence in a relatively short time.

In 1941 Emmart and Smith described their results with various strains of tubercle bacilli (3 human and 1 bovine) on the chorio-allantoic membrane of 9-day embryos. They concluded that the method could be used to evaluate the pathogenicity of various strains by noting the incidence of membranes with tubercles and the extent of tubercle development on the membranes following inoculation. They used 1 mg. of dried bacilli as an inoculation in each case. They appear to be the first workers, in connection with *B. tuberculosis*, to have suggested that the method of implantation on the chorio-allantoic membrane can be used to determine, within the short space of 6 days, the tuberculocidal action of a drug or its ability to alter the virulence of a given strain of tubercle bacilli.

The following year Burnet and Favis (1942) described a method for preserving membranes between lantern slides in glycerol-gelatin. We can vouch for the efficacy of the procedure. That same year Soltys (1942) published his work on the growth of avian, human and bovine tubercle bacilli in a medium containing 2 per cent. chick-embryo suspended in Tyrode's solution. The avian type of tubercle bacilli grew rapidly and was easily identified in every piece of tissue after 6 days. Moreover, it could be subcultured up to eight times. With bovine and human types the organisms multiplied but to a lesser extent than the avian tuberculosis bacilli, and, moreover, they could not apparently be subcultured.

In 1943 Emmart and Smith described their studies with the chorio-allantoic membrane as a medium to test the virulence of closely related strains of tubercle bacilli from the Trudeau Laboratories, Saranac Lake. Homogeneous suspensions of organisms in saline, containing 1·0 mg. tubercle bacilli dried weight, were used in each egg. Within 6 days after implantation of the membrane, 96 per cent. tubercle formation was present in the membranes implanted with the more virulent strain. The less virulent strain gave only 18 per cent. tubercle formation. They compared those results with guinea-pig inoculations. Only one guinea-pig inoculated with the avirulent strain died within 109 days, while 100 per cent. of those inoculated with the more virulent strain died within the same period. The authors concluded that the chorio-allantoic membrane of the chick-embryo can be successfully used to determine differences in virulence between closely related substrains of tubercle bacilli.

Fite and Olsen in 1944 described their results after inoculating 46 strains

of acid-fast bacilli on chick-embryo chorio-allantoic membranes. One finding, which is important in relation to our own observations, is that small doses of bacilli, 0·01 mg. or less, are by themselves inadequate to show characteristic changes in the membranes routinely. A good description of the histological appearances of the lesions is given. Their technique of membrane inoculation included the use of a hypodermic needle. Trauma with the point of this may have determined their finding, in 13 of 14 eggs examined, tubercle bacilli in the liver in portal areas and in endothelial and Kupfer cells. One of their conclusions was that the chorio-allantoic membrane varies too greatly in its response to avirulent acid-fast bacilli to make the procedure by itself of value in determining the virulence of a given strain or species of organism. The response of the chorio-allantoic membrane was constant for a given strain or species of organism and variations are chiefly in degree of individual eggs, not in type or overall extent of the lesions produced.

Developing eggs continued to be used in studying *Myco. tub.* and its growth. Emmart and Seibert in 1945 observed the inhibitory action of rabbits' serum on the formation of tubercles on 10-day chorio-allantoic membranes. The serum was from (*a*) sensitised animals high in gamma globulin and (*b*) from sera high in beta globulin from tuberculous animals. The conclusions in this involved work were that the gamma globulin fraction, rather than the beta, possesses the chief tuberculostatic properties.

Friedman in 1945 published an article on the lines of Solty's work. He grew tubercle bacilli in 3 days, in some cases, from sputum, tuberculous guinea-pig glands and lungs and from subcultures. The medium was 0·5 to 1 c.c. of minced 11-day chick-embryo in 25 c.c. Tyrode's solution; 300-500 units of pure penicillin were added. The inoculum was treated with 6 per cent. H_2SO_4 for 20 minutes and washed three times in sterile saline before being seeded into the culture medium.

Again in 1945 Emmart compared the tuberculostatic action of streptothricin and streptomycin on the chick-embryo chorio-allantoic membranes. Suspensions of bacilli and varying strengths of the drug were kept for 24 hours and then inoculated. The gross appearances of the membranes in the experimental and control groups were counted. The inhibitory effect of streptomycin on the development of tubercles on the chorio-allantoic membrane following incubation of bacilli with the drug at 37·5° C. for 24-48 hours was established.

In 1947 Lee and Stavitsky demonstrated that a rapid infection of the liver could be produced by inoculating chick-embryo intravenously with a standardised number of human tubercle bacilli. They showed that with streptomycin the lesions could be prevented from developing and they suggest the method as a screening procedure in chemo-therapeutic research because results are obtained in three weeks.

Present Investigations

Our investigations were undertaken in order to ascertain if chick-embryo culture had any place in the routine work of an ordinary bacteriological laboratory in a large sanatorium.

Methods.—We arranged through the Ministry of Food, Eggs Department, to have a dozen fertile eggs weekly from an accredited dealer. On five occasions

all the eggs were sterile. Apart from this the yield of fertile eggs was approximately 33 per cent. of those incubated. Thus at the start there is a big margin of waste.

Technique.—It was our practice to inoculate 10-day old chick-embryos and to chloroform and examine the embryo on the seventeenth day For chorio-allantoic inoculations the air space is marked by candling and a hole bored into it with a large dental burr, rotated between the fingers. A small triangle with half-inch sides is pencilled on the side of the egg at its broadest diameter and with the dental burr small holes are bored around the triangle through the shell but not through shell membrane. With a rigid, sterile needle the small triangle of shell is easily elevated and comes away, breaking from hole to hole. The spiral rim of the shell membrane fibres is noted and the membrane carefully split in that direction with the point of a sharp needle laid at right-angles to the direction of the fibres and depressed. Chorio-allantoic membrane lies beneath this and should not be harmed. A drop of fluid inoculum is placed over the slit in the shell membrane. By using a rubber teat and exhausting the air in the air space, the fluid inoculum acts as a fluid wedge and enters the egg, gently stripping chorio-allantoic membrane and spreading out over its surface. The open shell area is now covered with cellophane and the egg incubated.

Results

For the inoculations we made a concentrated emulsion of a ten-day smear culture of human tubercle bacilli on Lowenstein Jensen medium by agitating 2 platinum loopfuls of growth in 2 c.c. sterile normal saline, with glass beads. Subculture of the emulsion showed that the tubercle bacilli were viable. It is difficult to deal in terms of mgms. of dried tubercle bacilli in the average laboratory.

The first series of membranes, each inoculated with 4 large drops of this emulsion, yielded no tubercles. The tubercle bacillus, of human type, had been isolated from a German Jewess who had been ill for 4 years. She had a fairly constant chest X-ray appearance of mottling in all zones of each lung, worse at the apices, and no visible cavitation. There was bilateral, cervical, tuberculous adenitis (proved by biopsy) and axillary adenitis. She never produced sputum and her general resistance appeared from her history, clinical resistance, and serial X-ray appearances, to be high. The tubercle bacilli were obtained on a few occasions by laryngeal swabs and pulmonary lavage.

Failure with this strain of bacillus led us to use a strain from a young woman with progressing, cavernous phthisis. Clinically her condition was rapidly deteriorating. This emulsion yielded macroscopic tubercles in 25 per cent. of the membranes inoculated. The numbers of organisms were the same as with the first series of eggs used. It is tempting to think that we were dealing with a more virulent organism in the second case or one that had its virulence exalted by passage through a susceptible person. In the first case the bacillus may have been battling with a resistant host or it may have been of low virulence from the onset. Certainly the patient kept the upper hand of the disease during four years and the lungs showed no evidence of cavitation. Both strains

of tubercle bacilli were of human type as tested by rabbit inoculation. In guinea-pig lungs the tubercle bacilli from the first case produced several discrete, proliferative, tuberculous lesions and no caseation. The lesions were much less extensive than those produced by the tubercle bacilli from the second, rapidly deteriorating case of pulmonary tuberculosis. Guinea-pig lungs, after inoculation with tubercle bacilli from this latter case, showed massive areas of proliferative tuberculosis with occasional small caseous areas.

Figure 2 shows the macroscopic appearance of the tubercles on a chorio-allantoic membrane: (*a*) is an area with no tubercles, (*b*) is the part which was inoculated, and several tubercles are easily visible. Approximately 20 per cent. of embryos died within the 7 days after chorio-allantoic inoculation.

In virus work inoculations can be made into many sites—*e.g.*, the amnion (this, as used for influenza virus, infects the lungs), the allantois, the air space and yolk sac. Injections have been given by the intramuscular, intravenous and intracerebral routes as well as into the extra-embryonic body cavity. Using the hypodermic needle method described by Hirst to inoculate the amniotic cavity, we injected 0·2 c.c. of the tuberculosis bacilli emulsion through a tuberculin syringe. We were not able to produce tubercles in the embryonic lungs as we had intended. The method entails serial sectioning and histological examination of the tissues concerned. Fifty per cent. of the embryos so inoculated failed to survive seven days. Yolk-sac inoculation was done with 0·2 c.c. of the tuberculosis bacilli suspension. The method is easy and no fatalities of the embryo occurred before the seventeenth day. Smears of yolk stained by the Z.N. method showed tubercle bacilli, but in far scantier numbers than in the original suspension. We did not attempt intravenous inoculation.

A further use to which developing embryos may be put offered an opportunity of investigation during the course of this work. A patient with a mixed infection in a tuberculous empyema had received the relatively new drug Dibrompropamidine Isethionate intrapleurally to remove secondary contaminants. She was pyrexial before the drug was given. In three weeks acute yellow atrophy supervened and she died. In view of the initial pyrexia it could not be said that Dibrompropamidine Isethionate was responsible for the acute yellow atrophy, especially as other patients tolerated it. Various dilutions of the compound were tried on the 10-day-old chorio-allantoic membrane of developing chicks. 0·03 mlms. of 1 in 2,000 solution and 0·03 mlms. of 1 in 1,000 solution both produced a yellow, fatty-looking liver. The latter killed the embryo in 24 hours with hæmorrhages into the peritoneal cavity in addition; the former solution allowed the embryo to live for 7 days, when it was killed by us. Photo-micrographs of the liver from the human case (Fig. 3) and from the chick-embryo (Fig. 4) which lived for 7 days are produced for comparison. Both show fatty toxic changes. The result suggests that Dibrompropamidine Isethionate has distinct hepatotoxic properties and must be used with care in a pleural cavity. The dose of Dibrompropamidine Isethionate applied to the egg is, of course, a very different concentration from what one might expect would reach the liver when the drug was put into a human pleural cavity. In addition the developing chick liver would be almost certain to respond to any sort of toxic substance by fatty changes. Nevertheless, the experiment at least shows that the drug concerned does damage liver cells.

PLATE XV.

FIG. 1.

FIG. 2.

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PLATE XVI.

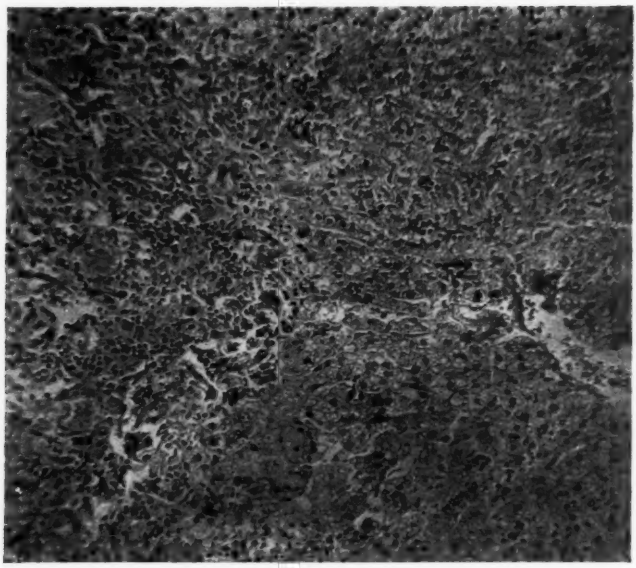

FIG. 3.

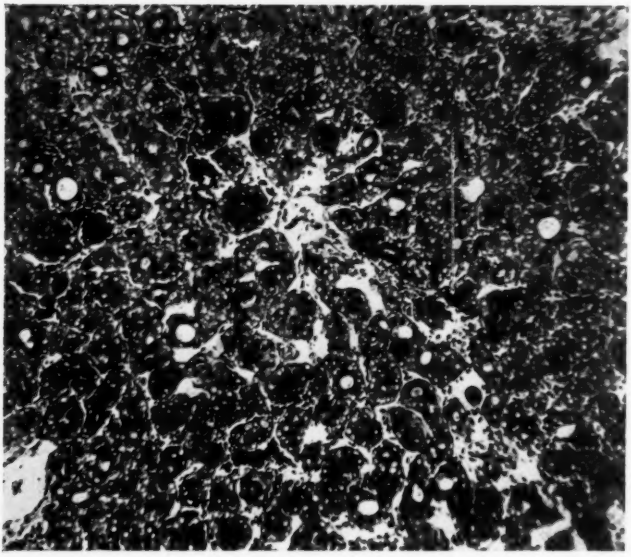

FIG. 4.

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Discussion

As a routine measure for culturing tubercle bacilli the developing chick-embryo is of no use and it will never replace the guinea-pig. It is of great academic use, however, and affords an interesting field of study. Large doses of bacilli must be used to produce lesions, and the developing embryo seems to be able to destroy large number of human tubercle bacilli. Diagnoses of C.S.F. and tissues with small numbers of tubercle bacilli cannot be done by inoculating embryos. Furthermore, when such specimens arrive at a laboratory, eggs at the correct stage of incubation are not always available. The trouble in obtaining eggs, and the cost when wastage is counted, make the method impracticable to-day. It is possible that differences in virulence of various strains of tubercle bacilli may be determined by chorio-allantoic inoculation methods. The two cases cited above indicate varying virulence of tubercle bacilli clinically, by guinea-pig inoculation and by chorio-allantoic methods. The use of sites of inoculation other than the chorio-allantois has not been uniformly successful in our hands and organ inoculation requires histological examination to assess results. The chick-embryo may be of great use to determine the toxicity of new chemo-therapeutic agents and the possibilities for new lines of research are numerous.

Summary

An outline on most of the work relating to the growth of *Myco. tuberculosis* in the chick-embryo is given. A brief description of the development of a chick-embryo is added. The technique of chorio-allantoic inoculation is described and the results given in a small number of trials. The use of eggs for testing the toxicity of new chemo-therapeutic drugs and the conclusions of our work are given.

Our thanks are due to Dr. G. H. Trayer, Medical Superintendent of Baguley Sanatorium, and to Dr. G. Stewart Smith, pathologist to the Manchester Corporation, for permission to carry out the work in the laboratory; and to Mr. Whittaker of the Ministry of Food, Eggs Department, for helping us to obtain a supply of suitable eggs.

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ALVEOLAR CELL TUMOUR OF THE LUNG:
Report of a Case

By R. I. McCALLUM

From the Brompton Hospital

The pulmonary condition known as malignant adenomatosis or alveolar cell tumour is held to be a definite pathological entity although its differentiation from other tumours in the lung is not universally accepted. Although it appears to be infrequent Neubuerger and Geever (1942) consider that this tumour is not so rare as has been thought hitherto. In a comprehensive review of the literature up to 1941 they selected 25 examples of definite alveolar cell tumours, and 15 others which they thought were controversial but which may well have belonged to this category. They preferred to use this term for the condition as it leaves open the question of histogenesis.

There have been relatively few reports of this tumour from Great Britain (Finlay and Parker, 1877, Gordon, 1920, Richardson, 1940, Dacie and Hoyle, 1943) compared with those from the United States of America, from where most of the recent papers have come. It has also been described in Germany (Löhlein, 1908, Oberndorfer, 1930) and South America (Sayago, 1932, Wenger, 1945). A further case of this type is here reported.

Case Report

An engineer-fitter, a male of 52 years, had been in excellent health for his age and had played tennis regularly until the summer of 1943. He worked out of doors much of his time and apart from winter coughs had no previous illness of note. There was nothing noteworthy in his family history. Until January 1945 he had been accustomed to smoking about 20 cigarettes a day and about 1½ ounces of pipe tobacco a week.

In June 1944 he had a chest cold with a cough and frothy sputum, and as symptoms persisted and there was some loss of weight he was sent by his doctor to a Tuberculosis Officer for radiological examination. An opacity was reported in the left lung, denser in the upper and middle zones. Pulmonary tuberculosis was suggested as the cause but as two specimens of sputum were found to be free from tubercle bacilli he was referred to the Brompton Hospital in May 1945 because a pulmonary new growth was suspected.

By this time he had lost about 1½ stone in weight, was slightly cyanosed and dyspnœic at rest and had a marked shift of the heart and mediastinum to the left with râles at the left base. Radiological examination showed patchy opacities throughout the whole left lung field particularly at the apex, suggesting collapse and consolidation mainly in the posterior part of the left upper lobe. There was relative emphysema of the right lung (Fig. 1). Bronchoscopy in July 1945 showed nothing abnormal apart from some pus in the orifice of the left lower lobe bronchus. His sputum contained only hæmolytic streptococci, staphylococcus aureus and Neisseriæ; no tubercle bacilli or malignant cells were found either in sputum or in a specimen of secretion obtained at bronchoscopy. His hæmoglobin was 116 per cent., with 6·1 million red cells, and his blood sedimentation rate was 4 mm./hr. (Westergren). He was admitted for further investigation in September 1945.

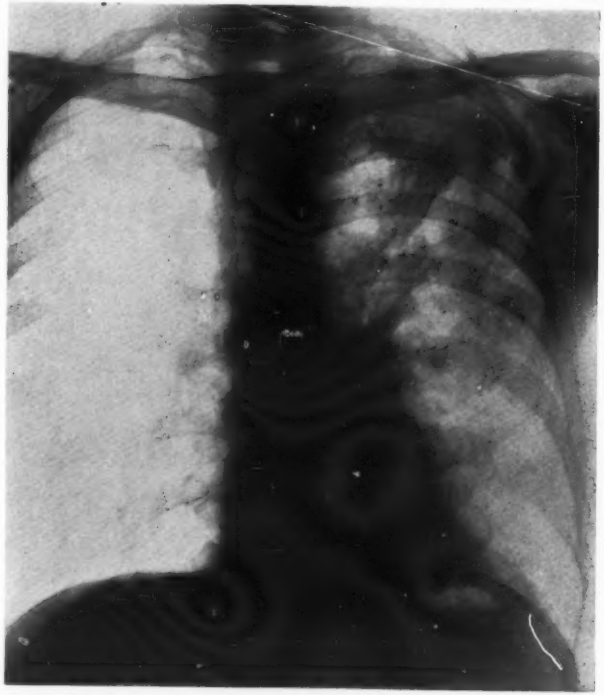

FIG. 1.

Alveolar Cell Tumour. Postero-anterior view of chest on 18.5.45, showing patchy opacity in left lung field and mediastinal shift to the left.

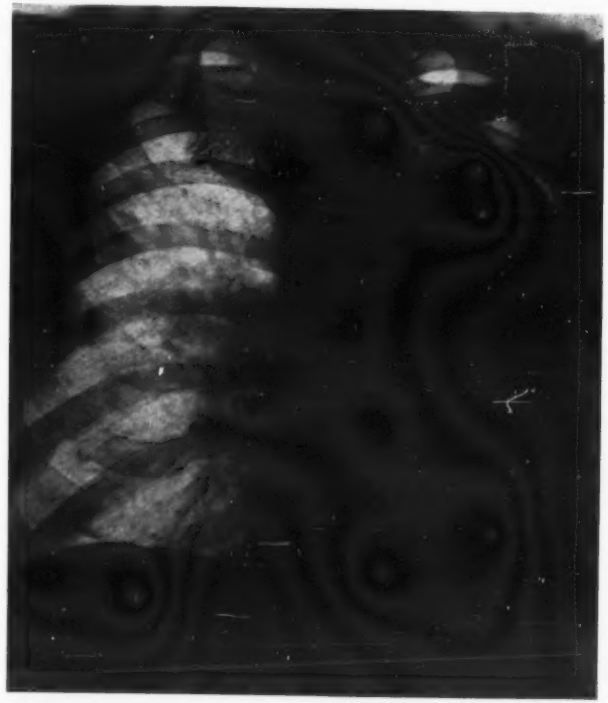

FIG. 2.

Alveolar Cell Tumour. Radiograph of 22.11.45, showing now an opaque left lung with spontaneous pneumothorax and an apical adhesion. The right lung has a congested appearance.

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PLATE XVIII.

FIG. 3.

Alveolar Cell Tumour. 31.12.45. The left pneumothorax is now obliterated by fluid and there is spread of the process to the right upper lobe.

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By then dyspnœa was more marked and he had himself noticed an increase in the blueness of his fingers and tips of his ears. While awaiting admission he had an acute pleurisy on the right side with slight pyrexia and small bright red specks of blood in his sputum, the only occasion in his whole illness on which this occurred. He was now bringing up about a cupful of thin frothy sputum in a day.

On examination he was an alert and intelligent man, spare but not emaciated, and there was marked congestion and deep cyanosis of his face and hands which became more pronounced with each paroxysm of coughing. With difficulty he produced profuse white frothy sputum. There was no finger clubbing and no abnormal findings other than those relative to his chest. The heart and trachea were displaced to the left, with dullness over the whole left chest and numerous fine crepitations from base to apex; breath sounds were diminished and there was bronchial breathing over a wide area of the left lung. Radiograms now showed some extension of the shadows on the left side.

Treatment was directed to relieving his anoxia and controlling his paroxysmal cough by continuous oxygen through a B.L.B. mask and linctus codeinæ in frequent doses.

Investigation now showed a hæmoglobin of 100 per cent., a red cell count of 5·4 million, and a leucocyte count of 11,200 with a normal differential count, B.S.R. 7 mm./hr. and blood Kahn negative. He had a vital capacity of 2,400 c.c. The circulation times were ether 7 secs., decholin 45 secs. A screen examination showed the diaphragm moving normally and together with radiograms failed to demonstrate any enlargement of the right heart, while a barium swallow showed a normal œsophagus. An E.C.G. showed regular rhythm with right axis deviation. The bones of the hands appeared normal on radiological examination. A second bronchoscopy could not be done as his condition deteriorated so rapidly.

Repeated microscopic examination and culture of his sputum failed to show tubercle bacilli, nor were B. Friedländer, fungi or malignant cells found. The organisms in the sputum were mainly penicillin-sensitive streptococcus viridans and staphylococcus aureus. The diagnosis was thought to be either a bronchial neoplasm or a chronic pneumonia, while malignant adenomatosis was considered as a rare possibility in view of a recently published case (Dacie and Hoyle, 1943).

Four days after admission he complained of pleural pain and local tenderness below the left nipple following a bout of coughing. The latter was becoming more severe and, together with cyanosis, increasingly difficult to control. Two days later his temperature rose suddenly to 103° F. and respiratory rate to 30 per minute. A full course of sulphadiazine was given, the temperature falling to 99° F., where it remained with some improvement in the general condition. A pleural rub appeared at the right base anteriorly with a patch of bronchial breathing posteriorly. A radiograph on 22.11.45 (Fig. 2) showed a large left pneumothorax with an opaque lung adherent at the apex. There was no fluid, the mediastinum was now central and the right lung had begun to take on a more congested appearance in successive films. Tomograms of the left lung showed it to be solid.

His condition remained much the same until early in December 1945 there was a further rise of temperature with increased dyspnœa and the appearance of signs in the right lung. Neither sulphadiazine nor penicillin had any effect. A film at this time showed a right midzone opacity extending from the hilum

to the chest wall and an effusion filling the left pleural space (Fig. 3). The fluid on examination showed a preponderance of red cells and lymphocytes and no organisms on direct examination or culture. Generalised œdema began to appear and he died suddenly on January 6, 1946.

Summary.—A previously fit man of 52 years complained of cough, frothy sputum, loss of weight and increasing dyspnœa from June 1944. X-ray of chest showed partial consolidation of all zones of the left lung with associated collapse. All investigations were negative including bronchoscopy. Symptoms gradually increased and the condition was complicated by a left spontaneous pneumothorax and effusion, and an acute spread of the process into the right lung before its fatal termination. There was no evidence of tuberculosis, fungus infection or syphilis, no neoplastic cells were found in sputum and neither sulphonamides nor penicillin had any effect upon the course of the illness.

Post-mortem Report

The body was examined 14 hours after death. The larynx and trachea appeared normal but the bronchi contained a small amount of frothy sputum. The left pleural cavity was completely obliterated by dense adhesions with the exception of a small pneumothorax about the size of a golf ball at the apex. These adhesions, although dense, were still active and fibrin was in the process of being organised. The right pleural cavity was free save for a band adhesion on the axillary surface of the right upper lobe.

Lungs.—The left lung was completely consolidated and felt very rubbery and firm. The consistency of this lung was much firmer than that of an ordinary pneumonic process. The right lung showed a well-marked example of an azygos lobe, and in addition the axillary part was consolidated and felt similar to the left lung. The rest of the upper lobe appeared normal, as did the middle lobe, but in the apical part of the lower lobe there were shotty areas of firm rubbery tumour similar to the areas of consolidation in the left lung. The tracheo-bronchial, broncho-pulmonary and mediastinal glands were not enlarged and appeared quite normal.

The pericardium was adherent to the left lower lobe but there was no pericardial effusion. Dilatation and slight hypertrophy of the right ventricle were found but this was less pronounced than had been anticipated from the patient's condition during life. The pulmonary artery and aorta showed no atheroma and appeared normal. No abnormality was found in the kidneys, ureter, bladder or suprarenals, and apart from some marked fatty change in the liver the whole of the digestive tract and glands appeared normal. The brain was not examined.

Histology.—Representative blocks taken from all areas of the left lung and the tumour areas of the right lung showed a uniform condition. This was quite characteristic of the so-called alveolar cell tumour and did not appear to differ in any way from cases previously reported. The bronchi in the affected areas show considerable inflammatory change and this extended also into the aerated portions of the lung. No secondary deposits of this tumour were found in any of the many glands or other organs of the body that were examined.

The microscopic structure of a portion of the tumour is shown in Figs. 4 and 5. The alveolar structure remains intact although the walls are thickened and covered by a layer of cuboidal cells which in places form papillary processes. The pleura was much thickened. No areas of carcinomatous degeneration were found in the sections taken.

PLATE XIX.

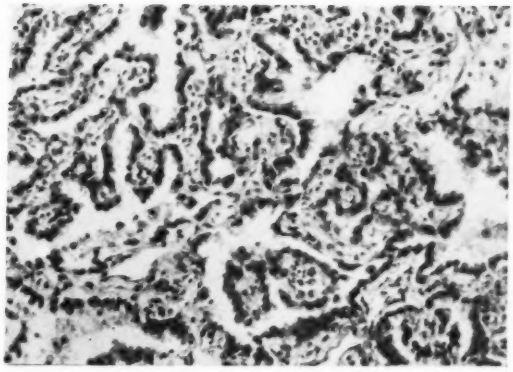

FIG. 4.
Alveolar Cell Tumour × 120, showing cuboidal epithelium lining alveoli.

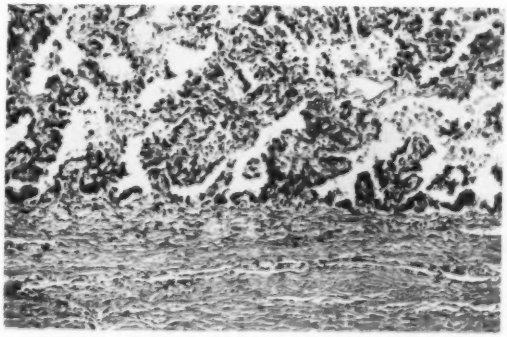

FIG. 5.
Alveolar Cell Tumour × 90, showing papillary processes and thickened pleura.

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Discussion

The condition in this patient corresponds to the diffuse form of adenomatosis described by Musser (1903). A nodular form was first reported by Malassez (1876), and is more common. The symptoms which have been described are characteristic of many reported cases. In this case also the clinical and pathological findings are in accordance with the criteria laid down by Neubuerger and Geever (1942), from which it appears to be a typical example.

Clinically there were unusual features which suggested that one might not be dealing with a bronchogenic carcinoma and they led to investigation to exclude other possible causes of the peculiar clinical and radiological picture. The lack of evidence of suppuration or lung destruction, the low erythrocyte sedimentation rate and normal white cell count, and the absence of marked cachexia in what was obviously an extensive pulmonary lesion were all remarkable. There were never any signs of metastatic deposits and the spread to the right lung was more like an infective process spreading into the upper lobe. This mode of spread is very similar to that in a case reported by Taft and Nickerson (1944), who showed a radiograph almost the same as Fig. 3. Although in our case alveolar cell tumour was considered before death, there were no means of proof and in view of its rarity it could not be thought a likely diagnosis. Wood and Pierson (1945) made the diagnosis by lobectomy in one case, a woman of 67 years, six months before death; but in our case the clinical condition rendered any surgical intervention impossible. A clinical diagnosis of alveolar cell tumour therefore presents great difficulties and practically all the reported cases have been diagnosed at autopsy or discovered incidentally where death was due to some other cause. Even where the condition is suspected a diagnosis of bronchogenic or metastatic carcinoma will most often be made, for age group and symptoms are similar.

The radiological picture is not sufficiently typical to enable a diagnosis to be made from bronchial carcinoma, chronic pneumonia, or pulmonary tuberculosis. Bronchoscopy does not appear to help except in demonstrating that there is no bronchial lesion in the visible bronchial tree to account for the signs and symptoms. The combination of symptoms, and evidence of cyanosis, dyspnœa and frothy sputum with radiologically diffuse or nodular shadows, without evidence of metastases, suppuration, tuberculosis or occupational risk, may at least lead to the inclusion of alveolar cell tumour in a differential diagnosis.

In considering the pathology of this condition two controversial subjects are raised: (i) Does such a tumour exist as a separate entity or is it in fact formed by a downgrowth of epithelium from a terminal bronchiole, that is, a bronchial new growth; and if it is a separate entity, (ii) does it originate in alveolar cells, and is there an alveolar epithelium?

In fœtal life an alveolar epithelium is present but disappears at about the end of the fifth month (Barnard and Day, 1937). After this point there is no general agreement as to the structure of the alveolar lining, if any. There are several current views (Herbut, 1944): (*a*) There is a continuous layer of epithelial cells (Gray's Anatomy, 29th Edn.); (*b*) there is a discontinuous layer of

undifferentiated cells of mesenchymal origin; (*c*) there is a discontinuous layer of epithelial cells; and (*d*) there are both mesenchymal and epithelial cells (Macklin, 1936). Miller (1947) is definitely of the opinion that there is an epithelium present but that it is difficult to demonstrate by the usual methods of study. He believes that as the alveoli become distended with the establishment of respiration the still continuous cuboidal epithelium of fœtal life becomes stretched so thin that the usual laboratory methods fail to demonstrate it. His work has been criticised in that he depended entirely on pathological material for his preparations and failed to discriminate between the reticulo-endothelial cells within the lung, which tend to mimic an alveolar lining, and a true epithelium (*Lancet*, 1947). Barnard (1943) does not consider that there is a continuous epithelial lining to the alveolus but that the scattered cuboidal cells found there are mesenchymal in origin.

If the alveolar cell tumour arises in the alveolus it is not clear from what source it comes; on the one hand it may originate in isolated cells of probable mesenchymal origin, or on the other hand it is the fœtal alveolar lining of epithelial origin which has never entirely disappeared that has produced it.

There is general agreement that in certain pathological conditions of the lungs an alveolar epithelium becomes demonstrable (Bell, 1943, Geever *et al.*, 1943, Herbut, 1944); in chronic passive congestion, lipoid pneumonia (Graef, 1939, Freiman *et al.*, 1940, Ikeda, 1935); bacterial pneumonias and also viral and chemical pneumonias, tuberculosis, syphilis (MacCallum, 1940); chronic inflammatory and fibrotic processes, and healing of lung wounds in the experimental animal (Montgomery, 1944); it also occurs in certain diseases of the lungs in animals.

Herbut (1944) supports the view that these cells arise as a downgrowth from the basal cells of the bronchiolar mucous membrane as in bronchiectasis and that the available evidence agrees with this. Miller believes that there is œdema and distension of the thin epithelium of the alveolar lining which then becomes demonstrable and is often pushed off the alveolar wall. Geever *et al.* (1943) claim that bronchial epithelial downgrowth is easily distinguishable histologically and that the epithelial cells are probably of mesenchymal origin. There is thus no general agreement on the presence or absence of alveolar epithelium, and this has an important bearing on the existence of a specific tumour in the alveoli such as has been described.

The origin of the cells of the so-called alveolar cell tumour is subject to the same diversity of view. They begin either in alveolar cells and are then epithelial or mesenchymal in origin, or else they arise as downgrowths from bronchiolar epithelium and are presumably multicentric in origin. It is of interest that Horning (1947) has recently reported work on the induction of tumours in lung tissue grafts by the application of carcinogenic compounds. The animals used were mice, and adult lung tissue was employed. In these experiments there was no reaction from the alveoli, but on the other hand the bronchiolar epithelium responded strikingly; this he regards as evidence against an alveolar epithelial lining. Willis (1948) also emphasises the great diversity of size, rate of growth, local spread and production of metastases in pulmonary carcinoma and thinks that it is unnecessary to postulate an alveolar origin; he considers that particular structural variants do not denote different

specific origins. Herbut (1944) considers it bronchiolar in origin, and Fried (1931) describes primary growth metastasising to other parts of the lung and lining the alveolar wall. On the contrary, Neubuerger (1942) believes that the alveolar lining develops under pathological conditions from mesenchymal cells and that there is a continuous developmental relationship between its occasional production in inflammation and the alveolar cell tumour. The mucus-producing characteristics of this tumour have been emphasised by Richardson (1940) and he considers this evidence of their bronchiolar source.

The difficulty of the apparent multicentric origin is explained by Weller (1929) as being more likely due to metastatic dissemination, and Willis would seem to support this view. No primary focus has been demonstrated in this type of tumour however and it is characteristic of it that secondary deposits are either absent or few and of small size. In our case it was unfortunately impossible to have serial sections and therefore the possibility of a point of continuity between the alveolar cells and bronchiolar epithelium was not excluded.

The balance of opinion is against an alveolar origin of this tumour and in favour of a bronchiolar one. There are still, however, points to be clarified.

The stimulus to such an overgrowth of epithelium is as obscure as in other forms of new growth. The similarity of the human disease to the condition known as adenomatosis, which occurs in sheep (Bonne, 1939, Dacie and Hoyle, 1942) and in other animals such as mice (McDonald and Woodhouse, 1942), horses and guinea-pigs, has attracted attention. In sheep proliferation of alveolar epithelium was described as a " white pneumonia " by McFadyean (1920) in association with *Strongylus rufescens* infestation. Cowdry (1925) described " Jaagsiekte " in South African sheep in which multiple foci of proliferation of alveolar epithelium appeared and spread into other parts of the lung without metastases. It was similar to the " progressive pneumonia " of sheep in Montana (Cowdry and Marsh, 1927), and the same type of lesion was also reported by Dungal (1938) in sheep in Iceland, where it arose in epidemic form. He found no relation to infestation, virus infection, or spirochætes, however. Infection seems certain in sheep, but in man there is no evidence that this is so and attempts to infect experimental animals from human material have failed (Wood and Pierson, 1945, Sims, 1943). Adenomatosis in man occurs only sporadically and rarely.

Wood (1943) has reported a case in which an alveolar cell tumour was found in association with lipoid pneumonia, and Graef (1939) describes swelling of the alveolar lining in lipoid pneumonia in which the epithelium, of ciliated columnar type, was traced as an extension from the bronchioles. In most reported cases of alveolar cell tumour there is no history of the continued use of oily nasal solutions or of mineral oil for constipation, and in our case there was no such history.

This type of tumour appears to be universally fatal in outcome through gradually encroaching on alveoli and rendering functionless large areas of lung. Even if it is considered that the conditions which have been described as malignant adenomatosis or alveolar cell tumour are in fact new growths of bronchial origin, as the balance of opinion favours, it still remains to be explained why they have spread in such a fashion as to line the walls of the

alveoli and why, with such widespread proliferation, there is generally no destruction of lung tissue and its structure can still be made out; and why no demonstrable focus of origin has yet been shown. In view of these characteristics a separate description of this type of growth is perhaps warranted.

Summary

1. A case of alveolar cell tumour is described.

2. Diagnosis presents great difficulty, as the picture is indistinguishable from that of bronchial new growth.

3. Certain unusual features in the course of the disease and negative findings on investigation may at least lead to the inclusion of this condition in the differential diagnosis.

4. The balance of opinion appears to favour a bronchiolar origin of the tumour, but its unusual characteristics warrant a separate description.

I am indebted to Dr. Clifford Hoyle for permission to report this case, to Mr. Price Thomas for the bronchoscopic report and to Dr. J. W. Clegg for the report of the post-mortem; also to the Department of Pathology, Royal Victoria Infirmary, Newcastle-upon-Tyne, for the micro-photographs.

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REVIEWS OF BOOKS

The Care of Tuberculosis in the Home. By James Maxwell. Second Edition, 1948. Hodder and Stoughton, London. Price 7s. 6d.

The inhabitants of sanatoria are notoriously inclined to think and talk about tuberculosis to the exclusion of more profitable subjects, and this disadvantage of self-knowledge weighs against the advantages to be gained from encouraging patients to understand their complaint. Nevertheless, in this disease above all others results depend so much on the co-operation of the patient that explanations are necessary, and indeed essential to counter the ghoulish tales that patients delight to circulate.

What does the tuberculous person need to know about his disease? Its essential nature and early manifestations, its dangers to himself and others, and what part he can play in combating these dangers; this probably covers his requirements, and most of the answers are to be found in this admirable little book. He does not need to know the indications for, nor the technique and complications of, the various available treatments, and these have been most wisely left out—with the exception of the rather questionable statement that thoracoplasty is never performed until pneumothorax has been tried and failed. Prevention of the spread of infection is well dealt with, and there is much sound advice on the problems of readaptation to normal life, including information about the financial assistance available during treatment and convalescence.

Dr. Maxwell manages to strike a very happy compromise between advising too much restriction of normal activities and over-optimism with regard to a rapid cure, and this book should do much to help the tuberculous patient to a sane and confident outlook, while also being of value to his doctor.

J. V. S.

Physical Signs in Clinical Surgery. By Hamilton Bailey, F.R.C.S. Eleventh Edition in 4 parts. Part I. John Wright and Sons, Ltd., Bristol. Price 8s. 6d.

The eleventh edition of this well-known book is being published at intervals in four paper-covered parts, in order, as the author maintains, to overcome the numerous difficulties and obstructions of present-day book production. The quality of the paper, illustrations and typography in this edition does not appear to have suffered in any way, and the excellence of the coloured photographs is as notable as in previous editions.

The first part covers some basic principles of clinical examination, and proceeds to the surgical conditions of the head. The ground covered is far from comprehensive, but the stimulus provided to painstaking and minute clinical examination is very commendable.

Tuberculosis. By F. M. POTTENGER, M.D., F.A.C.P. 1948. Pp. 597. Henry Kimpton, London. Price 60s.

This comprehensive work covers the field of pulmonary tuberculosis from all its aspects. The earlier chapters on pathogenesis present an orthodox and clear account of our knowledge up to the present day. The author's familiarity with the world literature is apparent, and each chapter is followed by a complete list of references. The endogenous source of reinfection-type phthisis is favoured, and its localisation to the postero-superior and apical portions of the lungs is explained on anatomical and physiological changes in the chest during the period of growth. The chapters on the clinical aspects of the disease can be recommended. The discussions on, and fearless criticism of, the usual physical signs in the chest are both welcome and stimulating. Great importance is attached to localised muscle spasm, restricted movement and atrophy of superficial structures as detected by inspection and " light touch palpation," and all are explained by irritative or trophic reflex activity. Those familiar with the author's extensive writings on the effects of visceral reflexes in disease will not be surprised to find two chapters of the book devoted to the visceral neurology of pulmonary tuberculosis. These chapters provide much food for thought and some for scepticism, but may help to explain various manifestations of the disease. It is felt that, as aids to diagnosis, their practical value is overrated, particularly when contrasted with the much smaller space devoted to X-ray examination of the lungs.

The general principles of treatment are discussed fully, and an optimistic note is struck throughout. An attempt is made to assess the importance of rest and exercise, open air, light therapy, and dietetic treatment. As a result of fifty years' experience, the writer has great faith in tuberculin as a therapeutic agent, particularly in genito-urinary and ocular tubercle, in other metastatic lesions, and also in many types of pulmonary disease. The failures of others are simply attributed to their lack of experience. " Compression " therapy is dealt with in twenty-four pages, pneumoperitoneum receiving a few lines only and extrapleural pneumothorax only a mention.

In the final chapters diagnostic and therapeutic problems are further illustrated by selected case reports, and a future programme is outlined with particular stress on mass radiography and B.C.G. vaccination.

The style is lucid and authoritative, with frequent subtitles; the book is well printed and produced, but some of the positive X-ray reproductions fall below standard. Representing, as it does, the results and conclusions of fifty years' experience, this book will command respect even from the most critical, and it can be recommended in particular to those wishing to broaden their outlook rather than extend their knowledge of tuberculosis. F. H. S.

NOTICE OF MEETING
JOINT TUBERCULOSIS COUNCIL

RECOMMENDATIONS which, if carried into effect, will affect every schoolteacher and other person employed in the care and education of organized groups of children are made in a report approved by the Joint Tuberculosis Council at their May meeting and shortly to be published.

The recommendations are based on the principle that all persons engaged in the care of organized groups of children shall be free from active pulmonary

tuberculosis. The risk of infection from adults is greater by far than the risk of milk, states the report, although this does not minimise the importance to children of a safe milk supply. Accordingly it is proposed to introduce strict clinical and radiological controls over teachers, doctors, nurses, nursery staffs and many other workers employed in schools, hospitals, institutions, nurseries, remand homes, orphanages and similar establishments.

The measures proposed are as follows:—

(1) No person with pulmonary tuberculosis should be allowed to accept employment which will involve contact with organized groups of children until the disease has been certified as arrested.

(2) All persons whose duties bring them into close contact with organized groups of children should at the time of their engagement undergo a medical examination including an X-ray examination of the chest, and they should thereafter be X-rayed annually while so employed. The cost of these examinations should be borne by the employer.

(3) If it is found that any employee is suffering from pulmonary tuberculosis, employment should cease at once and not be resumed until two consecutive medical certificates have been submitted, the first certifying that the disease is no longer active and the second stating that the improvement has been maintained for at least six months after the date of the first certificate.

(4) When employment is resumed, similar certificates should be submitted at three-monthly intervals for one year and at six-monthly intervals for a further two years.

An unusually high incidence of pulmonary or non-pulmonary tuberculosis in any organized group of children, says the report, should lead at once to a full investigation of the staff employed.

The report has been drawn up by a committee of the Joint Tuberculosis Council under Dr. Wilfrid Sheldon. Copies are expected to be available shortly.

At the same meeting the J.T.C. approved a report of a committee on the technique of chest radiography. This report will not be generally issued for a few months, as the Council are revising a pre-war publication on skiagraphic terminology and propose to publish this and the new report on technique as one document. Medical officers of regional hospital boards are, however, being told of the impending publication. The report (prepared by a committee under Dr. James Watt with the assistance of Dr. L. G. Blair as a co-opted member) assumes that within the next few years the bulk of chest radiography will be done on high-powered apparatus producing at least 400 milliamps. It states that the 15 in. × 12 in. film is the most useful single film for chest radiography, but recommends that each clinic should have at least two 17 in. × 14 in. cassettes with tanks to correspond.

A preliminary screening by the clinician or radiologist can be very helpful, it is stated, by furnishing information as to the movement of the diaphragm and the presence of emphysema. Allowance can be made for these in the postero-anterior view, and extra views can be added in any case of doubt.

The factors involved in a uniform technique of chest radiography are discussed, including the power of the equipment, the kind of tube employed, the use of a diaphragm, the duration of exposure, the tube-film distance, the positioning of the patient, the thickness of the subject's chest and the processing of film.

The Council decided to communicate with the Ministry of Health and with regional hospital boards regarding the employment of tuberculosis physicians jointly with local health authorities. Pointing out the importance of preserving intact the existing aspects of tuberculosis work—*i.e.*, the preventive, diagnostic, curative and rehabilitation aspects—the Council suggest that tuberculosis physicians should be employed by regional hospital boards and seconded as necessary to local health authorities for the preventive part of their work. The local authorities should pay the boards for these services, but there should be no direct employer-employee relationship between the local authorities and the physicians. The Council regard any possibility of dual employment as inimical to the efficiency of the tuberculosis service.

NOTICES

NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS

Commonwealth and Empire Health and Tuberculosis Conference, 1949. The Jubilee of the NAPT will be celebrated during 1949, and one of the principal functions in this connection will be the Commonwealth and Empire Health and Tuberculosis Conference at the Central Hall, Westminster, London, S.W.1, on July 5, 6 and 7. The programme will include the following subjects:

Tuberculosis as a World Problem.
Modern Treatment and its Results, including P.A.S. and Streptomycin.
Mass X-ray Methods: Their Evaluation and Scope.
Regional County Tuberculosis Schemes.
Organisation of Comprehensive Tuberculosis Schemes.
Organisation of Comprehensive Tuberculosis Schemes in British Colonies.
A Social Question (subject to be chosen later).
Tuberculosis among Nurses and Students.
The Eradication of Bovine Tuberculosis.

A fuller programme will be issued in the autumn.

NAPT Prize for Essay on Colonial Tuberculosis. A prize of one hundred guineas will be awarded for an Essay on THE CONTROL OF TUBERCULOSIS IN A BRITISH COLONY. The competition is open to doctors of either sex in the British Colonial Medical Service who are of not more than ten years', or less than five years' medical standing, of which at least three years have been spent overseas in a medical capacity.

Competitors should describe their own proposals for a practical scheme for the clinical, social and administrative control of tuberculosis, either in the British Colonies as a whole, or in one or more of them separately. Writers should give their own opinions based on personal experience of public health and anti-tuberculosis work.

Essays should reach Dr. Harley Williams, NAPT, not later than March 1, 1949. Award of the prize will be notified at the NAPT Commonwealth and Empire Conference described above. Essays shall become the property of the NAPT, and any of them may be published at its discretion in the author's name.

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NOTICES : : REVIEWS

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All manuscripts should be in a condition suitable for publication without further alteration. One galley proof will be sent to the author. All communications relating to papers submitted for publication should be sent to the Editor, Clifford Hoyle, 16 Marryat Road, S.W. 19. Other correspondence, including orders for reprints, which must be sent in by authors when they return their proofs, should go to the Publishers, Messrs. Baillière, Tindall and Cox, 7 & 8 Henrietta Street, W.C. 2.

NAPT Jubilee, 1949

COMMONWEALTH AND EMPIRE HEALTH & TUBERCULOSIS CONFERENCE

Central Hall, Westminster, London, S.W.1, 5th, 6th and 7th July, 1949

Provisional Programme:

TUBERCULOSIS AS A WORLD PROBLEM — TRENDS IN THE MODERN TREATMENT FOR TUBERCULOSIS — REGIONAL COUNTY TUBERCULOSIS SCHEMES — ORGANISATION OF COMPREHENSIVE TUBERCULOSIS SCHEMES—PROBLEMS IN THE PREVENTION AND DEFECTION OF TUBERCULOSIS (a) Tuberculosis among Nurses and Students (b) The Policy of B.C.G. Administration — THE PSYCHOLOGY AND SOCIAL RE-ADAPTION IN INDUSTRY — PROTECTION FROM BOVINE TUBERCULOUS INFECTION

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